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| EXAMINER | |
|---|---|
| WOITACH, JOSEPH T | |
| ART UNIT | PAPER NUMBER |
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Please find below and/or attached an Office communication concerning this application or proceeding.

File

# Office Action Summary

| Application No. | Applicant(s) |
|---|---|
| 09/885,679 | Pera, M. |
| **Examiner** | **Art Unit** |
| Joseph Woitach | 1632 |

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) ☒ Responsive to communication(s) filed on *Apr 24, 2003* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

**Disposition of Claims**

4) ☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above, claim(s) *16-24, 28, and 30-37* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-15, 25-27, and 29* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

**Application Papers**

9) ☒ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on *Jun 20, 2001* is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☒ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 5
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

This application filed June 20, 2001 claims benefit to foreign applications PR1327, filed November 8, 2000, and PQ8242, filed June 20, 2000, both in Australia.

Applicants' amendment filed December 9, 2002, paper number 8, has been received and entered. Claim 5 has been amended. Claims 38-44 have been canceled. Claims 1-37 are pending.

### *Election/Restriction*

Applicant's election with traverse of group I, and the election of species of noggin in Paper No. 11 is acknowledged. The traversal is on the ground(s) that the inventions as grouped by the Examiner are not "independent and distinct" as to justify the restriction requirement (applicants' amendment top of page 4). Specifically, Applicants summarize the basis for the office to make a restriction requirement and argue that "[T]he undifferentiated ES cells cultured in accordance with the present invention are capable of undergoing somatic differentiation to product progenitor cells and somatic cells. Therefore, the undifferentiated ES cells, the progenitor cells and the somatic cells prepared from such undifferentiated ES cells, as well as methods for preparing and culturing these cells, are related to each other as different aspects of a single invention" (middle of page 4). Additionally, Applicants summarize the findings of the court to include several aspect of an invention together citing *In re Kuehl* (bottom of page 4), that

the classification of groups does to establish independence and distinctness (page 5), and that continued increases in official fees provides a potential limitation to Applicants' resources and is contrary to the constitutional purpose of the patent system and regulatory changes of GATT (bottom of page 5 through page 6). Finally, Applicants point out that restriction must be made to independent and distinct inventions otherwise it may raise legal challenge alleging double patenting.

This is not found persuasive because Applicants fail to point to what single invention encompasses the groups set forth in the restriction requirement as only different aspects of a single invention. Initially, no argument is presented to why group III, an insulin or insulin induced factor, is related to the methods set forth in Groups I and II. With respect to Groups I and II, methods of obtaining pluripotent stem cells and methods of obtaining differentiated somatic cells are different and distinct because as set forth in the restriction requirement the different methods require different materials to practice, require different method steps to practice, and result in a materially different products. There is no single invention or inventive concept which unites these materially different methods as simply different aspects of one invention. As such, the findings of *In re Kuehl* are not applicable because the different methods are not different aspects of a single invention in different classes, rather they are different inventions. The different inventions of groups I and II have the same class and subclass, and Examiner agrees that classification alone may not constitute the basis for requiring a restriction. However, classification is only one criteria for determining distinctness, and in this case the

search of the non-patent literature and key word searches of even the patent literature would not be co-extensive because the different inventions comprise the use of different materials and different method steps to practice. Importantly, search and consideration of the conditions for differentiating a cell are opposed to the conditions for maintaining a cell in an undifferentiated state. Applicants' arguments that the claims are drawn to different aspects of single invention are not found convincing because the methods encompassed by the Groups I and II are directed to two diametrically opposed methods. With respect to the remaining arguments, Examiner acknowledges the requirement for the payment of official fees however this is not material in making a restriction requirement. Furthermore, because the inventions are independent and distinct they would not be subject to double patenting.

With respect to the election of species, Applicants have not provided any arguments in traverse on the ground that the species are not patentably distinct, nor has applicant submitted evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. Further, Applicants have noted that claims 1-15, 25-27 and 29 read on the elected species of noggin (page 3). Therefore, it is maintained that the various species represented by structural different antagonists are unique and distinct species.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-37 are pending. Claims 16-24, 28 and 30-37 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there

being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 11. Claims 1-15, 25-27 and 29 are currently under examination as they are drawn to methods of culturing ES cells with the BMP antagonist noggin.

***Priority***

Acknowledgment is made of applicant's claim for foreign priority based on applications PR1327 and PQ8242 filed in Australia on November 8, 2000 and June 20, 2000, respectively. It is noted, however, that applicant has not filed a certified copy of the Australian application as required by 35 U.S.C. 119(b). Accordingly, priority date of the instant application is its filing date June 20, 2001.

***Specification***

The abstract of the disclosure is objected to because it is not present as a single paragraph. Correction is required. See MPEP § 608.01(b).

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form limited to a single paragraph on a separate sheet within the range of 50 -150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

***Claim Objections***

Claim 29 is objected to because of the following informalities: Claim 29 is dependent on claim 28 which is a claim withdrawn from consideration. The claim should be amended to reflect the elected invention. Appropriate correction is required.

***Double Patenting***

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claim 25 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 3. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP §

706.03(k). In the instant case, claims 3 and 25 are duplicates and encompass exactly the same method steps.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 3-9 and 25-27 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 13-15 and 20 of copending Application No. 09/670,198. Initially, it is noted that in 09/670,198 Applicants have elected

methods of culturing pluripotential cells and compositions for practicing said methods (see restriction requirement, paper number 6, and election paper, number 8). Although the conflicting claims are not identical, they are not patentably distinct from each other because in each case the methods are drawn to methods of culturing comprising the same steps and using noggin as an antagonist/inhibitor of the BMP pathway. Each set of claims set forth obtaining a source of pluripotential cells and the dependent claims of 09/670,198 specifically recite that ES cells are a contemplated source. Further, each set of claims set forth inhibiting the BMP pathway, and in each application dependent claims specifically set forth that the agent used is noggin.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4-12 and 25-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of culturing human embryonic stem (ES) cells comprising: (1) obtaining a source of human ES cells; and (2) providing culturing conditions of said human ES cells in the presence of noggin for 5 days wherein said conditions result in an undifferentiated cell which does not express ES stem cell markers, does not reasonably provide

enablement for methods using the ES cells of any species of animal or for producing progenitor cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice and make the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The basis of the instant rejection focuses on two main aspects of enablement. First, the ability of using and practicing the instantly claimed method in ES cells other than from those

obtained from humans. Second, the nature of the resulting cells after practicing the specific method steps of culturing ES cells with an antagonist of a BMP pathway, in particular treating the cells with the elected species of noggin. At the time of filing, the affects of noggin on the BMP pathway were known. Valenzuela *et al.* (US Patent 5,843,775) describe the cloning of frog, mouse and human noggin sequences (provided in sequence listing). Carpenter *et al.* teach that noggin is capable of inducing dorsal development in vertebrates when expressed (column 4, lines 64-67) and that noggin is a neurotrophic factor (column 5, lines 39-42). In the characterization of recombinant human noggin, Carpenter *et al.* demonstrate that noggin alone is capable of driving neuronal induction in developing embryos (column 25, lines 15-50; and results summarized by figures 4 and 6). Subsequently, as summarized in Shou *et al.* (Dev. 127, 5403-5413), the role of specific BMP family members and there antagonists is a complex and interactive pathway. In development, Shou *et al.* teach that "BMPs exert both ligand-specific and concentration-dependent effects on neurogenesis" and that "opposing effects (cell death and survival) are exerted at different cell stages in neuronal lineages" (page 5404, top of first column). Thus, at the time of filing, noggin was known in the art to be a neurogenic factor affecting BMP-2 and important in neuronal differentiation.

The present specification proposes that because stimulating BMP-2 in ES cells results in neuronal differentiation, using the antagonistic noggin to affect BMP-2 signaling in ES cells would prevent differentiation of said ES cells. The present specification provides one working example wherein using human ES cells cultured in the presence of noggin for 5 days, an

undifferentiated cell type lacking stem cell markers can be observed (page 28). Because of the lack of neuronal markers, the specification teaches that resulting cells are not neuronal progenitor cells (page 29, lines 15-16), however the specification acknowledges that the "identity and differentiation potential of the cells induced by treatment of human ES cells with noggin has yet to be defined" (page 29, lines 17-19).

With respect to the ability of noggin to affect any type of ES cell in culture, while it was clear from the prior art that noggin has a role and can influence development of neurons in the animals studied, Finley *et al.* (IDS reference) teaches that the ability of noggin to affect cells in culture, in particular mouse embryonic stem cells, was not directly correlative to these observations. Importantly, Finley *et al.* report that noggin alone had no affect on the differentiation of mouse ES cells during neuronal or glial differentiation (summarized in abstract, last two lines; and detailed page 273, first column). Mehler *et al.* (Dev. Neurosci. 22:74-85) teach that role of BMPs and there antogonist is complex and progressive in affecting both differentiation and the viability of cells during differentiation (summarized in abstract). With respect to the affects of noggin, Mehler *et al.* teach that noggin affects the percent survivability of mouse ES cells during differentiation as measured by the number of oligodendrocytes generated (figure 3). The specification provides evidence that human ES cells cultured with noggin for 5 days result in a cell which no longer expresses stem cell markers. Further, the specification demonstrates that the resulting cells are capable of differentiating into neuronal lineages, and interpreting the results it asserts that it is not simply a neuronal stem cell as evidence by the lack

of neuronal markers. Clearly Finley *et al.* teach that simply supplying noggin to mouse ES cells has not affect, however the working example provided in the instant disclosure indicates that human ES cells cultured with noggin are affected. Importantly, it is known in the art that ES cells differ from species to species, in particular human ES cells differ in there *in vitro* requirements as compared to ES cells from mouse, rat or hamsters (see summary in Thomson US Pat 5,843,780, column 12, lines 40-51). Culturing human ES cells for 5 days in the presence of noggin results in a unique cell type which has not been described in other species, however given the evidence of record, it does not appear that what is observed with human ES cells will extend to any other ES cell obtained from other species.

With respect to the using the methods as instantly claimed for producing "a progenitor cell", as noted above, the specification acknowledges that treating human ES cells with noggin results in a cell has not been fully characterized. Lacking neuronal cell markers the specification asserts it is not a neuronal progenitor cell. The specification provides evidence that the noggin treated human ES cell are capable of differentiating into neuronal and glial cells. Further, the specification teaches that the resulting noggin treated human ES cell can be used for a "facile route to the isolation of neuronal progenitors" (page 29, lines 13-14). In light of the lack of neuronal markers and the lack of stem cell markers, the noggin treated cell appears to be an intermediate cell type. The ability of the resulting cell to differentiate into neuronal cell types is consistent with the activity previously known and described for noggin and BMP-2. However, based on the differences between mouse and human ES cells it can not be excluded that the

human ES cell treated for 5 days with noggin results in a cell which is capable of differentiating into other somatic cell lineages besides that of neuronal origin. The courts have stated that reasonable correlation must exist between scope of exclusive right to patent application and scope of enablement set forth in patent application. 27 USPQ2d 1662 *Ex parte Maizel.* In this case, practicing the claimed methods is facile, however given the lack of characterization of the resulting noggin treated cell as acknowledged by the specification there is not objective evidence that the resulting noggin treated cell is a progenitor capable of giving rise to any somatic lineage. Given the complexity of the BMP pathway recognized in the art and the affect of noggin on ES cells from other species, the only defining character of the resulting cell considered adequately defined would be the cell lacking the original ES cell markers. As taught by the specification this noggin treated cell type can be used to produce neuronal progenitor cells.

In summary, the specification provides evidence that human ES cells treated with noggin for 5 days results in a cell lacking the original stem cell markers and guidance to use this resulting noggin treated cell to produce neuronal progenitor cells and potentially other cell types. However, the role of noggin in human ES cells is contrary to the affect of noggin in ES cells from other species and to its role in controlling neuronal differentiation. Given the guidance in the specification and the evidence of record, only methods of culturing human embryonic stem (ES) cells comprising: (1) obtaining a source of human ES cells; and (2) providing culturing conditions of said human ES cells in the presence of noggin for 5 days wherein said conditions result in an undiffernetiated cell which does not express ES stem cell markers are enabled.

In view of the lack of guidance, working examples, breadth of the claims, the level of skill in the art and state of the art at the time of the claimed invention was made, it would have required undue experimentation to make and/or use the invention as claimed.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 13-15 and 29 are rejected under 35 U.S.C. 102(b) as being anticipated by Thomson (US Patent 5,843,780).

Claims 1, 2, 13, 15 and 29 are drawn to and encompass undifferentiated ES cells, and claims 14, 15 and 29 are drawn to and encompass a progenitor cell. It is noted that a progenitor cell is not specifically defined in the specification, however within the context of the methods the term is described as a "cell which is capable of differentiation into any somatic lineage" (page 14, lines 24-26). The term "progenitor cell" as recognized in the art is a general term which is

consistent with that set forth in the specification as indicated above, and for the purposes of art rejections is being interpreted by the functional ability of the cell to give rise to any somatic cell lineage. In this case, because embryonic stem cells are capable of giving rise to any somatic cell lineage, an ES cell is being interpreted to be a type of progenitor cell.

Thomson teach primate embryonic stem cells. The stem cells are pluripotent capable of giving rise to the various somatic cell lineages which is demonstrated by injecting the cells into a SCID mouse and analyzing the resulting cell types (column 11, lines 12-58). Thus, the anticipate the ES/progenitor cells encompassed by claims 1, 2 and 15. With respect to the specific antibody markers set forth in claim 15, it is noted that Thomoson does not specifically analyze for the presence or absence of these cell surface markers, however as recognized in the art and indicated in the present specification they represent markers on ES cell cultures which are allowed to spontaneously differentiate and are present at early time points of 7-10 days in culture (page 13, lines 20-30). Because the primate ES cells described by Thomson are highly pluripotent and not subject to differentiating conditions in culture, they would not have any of these cell surface markers.

Moreover, with respect to the ES cells as claimed as a product by process (claims 13, 14, 29 and in part 15), where, as here, the claimed and prior art products are identical or substantially identical, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. Whether the rejection is based on "inherency" under 35 USC 102, or "prima facie obviousness" under 35 USC 103, jointly or

alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown,* 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). With respect to the methods wherein the ES cells are cultured in the presence of noggin or where noggin is used to produce a progenitor cell, any particular affect of these methods on the ES or resulting progenitor cell to differentiate from that known in the art is not set forth. Therefore in this case, the undifferentiated ES cells and progenitor cells being claimed are being interpreted to be cells defined by their functional properties which are cells capable of giving rise to any cell type of any lineage. As noted above, Thomson teach that the primate embyronic stem cells are pluripotent and capable of giving rise to the various somatic cell lineages which was demonstrated by injecting the ES cells into a SCID mouse and analyzing the resulting cell types (column 11, lines 12-58). Since the ES cells described by Thomson have the phenotypic characteristics of ES/progenitor cells recognized in the art as defined and supported by the instant specification, the primate ES cells described by Thomson anticipate the instantly claimed ES/progenitor cells which were cultured in the presence of noggin.

Claims 1, 2, 3, 13-15 and 29 are rejected under 35 U.S.C. 102(e) as being anticipated by Carpenter *et al.* (Pub. No. US2002/0019046 A1).

Claims 1, 2, 13-15 and 29 are summarized above. Briefly, claims 1, 2, 13, 15 and 29 are drawn to undifferentiated ES cells, and claims 14, 15 and 29 are drawn to and encompass a

progenitor cell, and that the term "progenitor cell" for the puproses of art rejections is being interpreted by the functional ability of the cell to give rise to any somatic cell lineage. As discussed above, because embryonic stem cells are capable of giving rise to any somatic cell lineage, an ES cell is being interpreted to be a type of progenitor cell. Carpenter *et al.* teach primate pluripotent stem cells, and specifically teach that embryonic stem cells as taught by Thomson (page 4, paragraphs 45-48, in particular paragraph 46). Thus, to the extent that the instantly claimed products encompass embryonic stem cells, the pluripotential embryonic stem cells taught by Carpenter *et al.* anticipate claims 1, 2, 13-15 and 29.

Claim 3 is drawn to a method of culturing undifferentiated ES cells. The method steps require obtaining embryonic stem cells and culturing them in the presence of the elected species of noggin. Carpenter *et al.* teach methods for directing the differentiation of ES cells into various specific somatic cell lineages. In particular, Carpenter *et al.* teach using TGF-β antagonist noggin for generating neurons (conditions set forth in Table 3-Group 5; and results summarized in paragraph 207). The method and conditions set forth in claim 3 simply require providing ES cells and culturing them in the presences of noggin, thus the methods of differentiating primate ES cells into neurons by culturing the cells in the presences of noggin anticipate the method set forth in claim 3.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Ratsch *et al.* (Dev. Biol. 245, 83-94 (2002)) provide further post-filing evidence for the complexity of the BMP pathway and the role of noggin in affecting differentiation in mouse ES cells.

Goldman *et al.* (US Patent 6,245,564) provide evidence that other types of progenitor cells were known in the prior art. Specifically, Goldman *et al.* disclose the isolation and characterization of neuronal progenitor cells. While the neuronal progenitor cells, as well as other tissue specific progenitor cells known in the prior art, may not be derived from ES cells directly, tissue specific progenitor cells would anticipate the compositions as instantly claimed because they are capable of giving rise to various somatic lineages.

***Conclusion***

No claim is allowed. Claims 4-12 and 25-27 are free of the art of record because while the art teaches that noggin is important as an agonist in the BMP pathway, it does not teach that noggin should be used to maintain cultures of ES cells or to produce progenitor cells. Though the prior art does not anticipate the claims, the claims are subject to other rejections.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (703) 308-2141.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703)308-4242 and (703)305-3014.

Joseph T. Woitach

Joe Woitach
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